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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,017	07/26/2001	Arrigo DeBenedetti	00S08 DeBenedetti	8138

26874 7590 08/27/2003  
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EXAMINER
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ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	14

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/916,017	DEBENEDETTI ET AL.
Examiner	Art Unit	
J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM

THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 23 June 2003.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-16 and 18-27 is/are pending in the application.

4a) Of the above claim(s) 1-9 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 10-16 and 18-27 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) Notice of References Cited (PTO-892)                            4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                    5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.                    6) Other: \_\_\_\_\_ .

**DETAILED ACTION**

1. This Action is in response to the communication filed on 6/20/03, as Paper No. 15. The amendment has been entered. Claim 17 has been cancelled. Claims 1-16 and 18-27 are currently pending in the application and are addressed herein.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

***Election/Restrictions***

3. Claims 1-9 have been previously withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention for the reasons of record, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 4.
4. Claims 10-16 and 18-27 are examined herein.

***Miscellaneous***

It is noted that Applicants representative was contacted regarding the remaining issues set forth herein (see attached interview summary). Applicants were informed of the problems with respect to "stability of  $\Delta G$ " values present in the claims and the problem associated with the UTR of ODC in claim 12. Applicants agreed to submit a response to these issues by fax, but as of 8/25/03, the fax has not been matched with the file, necessitating the issuance of this Action.

***Claim Rejections - 35 USC § 112***

5. Claims 10-16 and 18-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. The instant claims are drawn to A DNA sequence comprising a promoter operatively linked to a transcription sequence; wherein the transcription sequence, when transcribed produces a messenger RNA sequence that comprises a translated sequence encoding a toxin and an untranslated sequence... wherein the untranslated sequence further comprises a hairpin secondary structure conformation having a stability of  $\Delta G \geq$  about 50 Kcal/Mol. (Emphasis added; e.g., see claim 10 and claim 21).

Claim 12 indicates that the untranslated sequence comprises, among others, the 5'UTR of ornithine decarboxylase (ODC).

However, Applicants have indicated in the Declaration (under 37 CFR 1.132) filed 6/23/03 that the 5'UTR of ODC utilized by Shimogori did not comprise a hairpin secondary structure conformation having a stability of  $\Delta G \geq$  about 50 Kcal/Mol. In fact, Applicants indicated that the 5'UTR of ODC utilized by Shimogori only forms a structure having a stability of  $\Delta G$  of about -22 Kcal/Mol.

This presents two problems. First, it is unclear how claim 12 can encompass the 5'UTR of ODC when the Declaration clearly indicates that the 5'UTR of ODC forms a structure that is not sufficient to inhibit translation in the absence of eIF4E. Second, the fact that the Declaration

indicates that the 5' UTR structure of ODC described by Shimogori forms a secondary structure having "a stability  $\Delta G$  of about -22 Kcal/Mol. This appears to be inconsistent with the terminology related to the stability of the secondary structure set forth in claims 10 and 21, wherein the untranslated sequences comprise a secondary structure having a stability of  $\Delta G$  of about 50 Kcal/Mol (i.e., a positive value). Since the instant claims (see claims 10 and 21) indicate that the stability of the secondary structure is expressed as a  $\Delta G$  having a positive value and the Declaration refers to the stability as  $\Delta G$  having a negative number. Without a clear indication that the 5'UTRs encompassed by the claims form a structure having positive or negative  $\Delta G$  values (i.e. free energies); one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation.

Claims 11-16, 18-21 and 22-27 are dependent claims and are rejected for the same reasons.

It is noted that the Applicants have agrees to submit a response comprising an explanation for why the 5'UTR of Shimogori is distinct from the 5'UTR set forth in claim 12; and also to better explain  $\Delta G$  value (free energy) with respect to the secondary structures formed by the 5'UTRs of the claims.

It is noted that the claims, as they are presently, are free or the prior art. Clarification of the free energy ( $\Delta G$ ) with respect to the 5'UTRs encompassed by the claims would obviate the pending rejections.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell  
Patent Examiner  
AU 1635

  
DAVE T. NGUYEN  
PRIMARY EXAMINER